UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,912	08/28/2006	Timo Heinrich	MERCK-3230	4395

23599 7590 12/18/2009

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
CHANG, CELIA C	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
12/18/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@mwzb.com

Office Action Summary	Application No.	Applicant(s)	
	10/590,912	HEINRICH ET AL.	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *01 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *5,7 and 8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of group I in the reply filed on Sept, 1, 2009 is acknowledged. The traversal is on the ground that the office has not provided reasoning for the burden in searching all the claims. This is not found persuasive because preparation of medicament is not limited to a single active ingredient but includes multiple active ingredients which is not coextensive as search compounds per se. It was evidenced in the previous office action that the method can be practiced with materially different product, thus, the independence and distinctness was supported. The search for such diverse subject matter including different class and subclass and different scope in electronic search evidenced extreme burden if restriction was not required.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-4 and 6 are prosecuted. Claims 5, 7-8 are withdrawn from consideration per 37 CFR 1.142(b).

2. Claims 1, 3 or 4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims encompassed the scope of "solvates of the compounds" for which no description or enabling support can be found in the specification. Please note that each solvate is a different "chemical identity" and there should never be any doubt in this century as to the chemical identity of a material (see Suddon). Unlike formation of salts between a pharmaceutically acceptable acid and an organic base compound of the claims, the formation of "solvates" must find descriptive and enabling support for such claimed scope because absent of specific description, one having ordinary skill in possession of compounds would not be able to offer any predictability of which one will form what solvate (see Braga p.3640). A survey of the specification indicated there is no description of which solvent can form solvate with the compounds, under what condition will such solvates be obtained, and whether the solvates will

have consistent properties to be considered inclusive as being a "Markush" alternative of the compounds.

No examples, no process of making, no starting material or operability can be found for any compound encompassed by the Markush formula to have the ability in forming what solvate. Therefore, absent of description and enabling disclosure, the specification is insufficient in supporting the "claimed" scope of "solvates of the compounds".

3. Claims 3-4 are objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Please note that if the scope of claims 3-4 are "compounds". The innate nature or properties of the compounds are not limiting. It is also very confusing what does "as medicaments" mean. Does it mean being active i.e. only when it is exerting a biological activity? Does it mean a therapeutically effective amount? It is recommended that if the claims are further limiting of the compound claim 1, the specific structural limitation should be incorporated. If the claims are compositions, then, specific quantitative limitation should be incorporated and dependent on claim 6.

4. Claims 1-4, 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916), where the Supreme Court looked to whether the experimentation needed to practice an invention was undue or unreasonable. *Id.* An invention must be described so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*,

858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988). As stated in the MPEP 2164.01(a) "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". The analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole. *Id.* at 740, *Id.* at 1407. The factors to be considered herein are those set forth as the In re Wands, 8 USPQ 2nd 1400 (1988) decision.

The analysis is applied to the instant case.

Nature of invention

The claims are drawn to compounds of formula I, racemates, enatiomers, diastereomers, salts or solvates, having $5HT_{2A}$ antagonistic activity.

Breadth of the claims

A very large number of compounds are included in the scope of formula I with additional heterocyclic moieties and diverse structure.

The state of the art and predictability

It is well recognized in the art that receptor binding is structural sensitive requiring size, charge and stereo-specific chemical structure. The art recognized that for a specific receptor, some prediction and be made by modifying a pharmacophore of known receptor binding compounds (see Awadallah et al. whole article).

Level of ordinary skill

Prior art in the filed of indolylpiperidinyl compounds which having similar structure as those of claim 1 are known to be 5HT6 receptor binding (see Zhou et al. US 6,815,456, Kim CA148:92237, Ramakrishna CA150:329617). Currently, the pharmacophore for $5HT_{2A}$ has been evidenced by Sobrio et al. Smith et al. or WO 99/11641 (cited on 1449), which have the piperidinyl moiety attached on the 5-membered ring of the indolyl moiety.

Amount of experimentation/guidance

Structural-activity relation studies with respect to pharmacophore prediction indicated that only limited variation of a pharmacophore will maintain its biological activity (see Stiefl et al.) even with the help of extensive computerized tools.

Working examples

The specification provided no data on how the compounds can selectively and specification bind the 5HT2A receptor. It is well recognized in the field that 5HT2A antagonists are effective in treating psychosis but non-specific binding results in side effects and long term damage (see Wikipedia). In absence of any factual evidence, the specification provided no guidance as to forming dosage in the effective yet non-toxic range for therapeutic use.

In addition, no nexus was found in the specification or the record that such chemical structure of formula I would have activity from preventing blood clot/infarction of the brain (cerebral ischemia etc.) to eating disorders, to memory disorders etc. Nor was there any nexus in the record that 5HT2A antagonism is the mechanism for such diversified physiological dysfunctions found in Parkinson's disease, amyotrophic lateral sclerosis, premenstrual syndrome etc.

In view of the complexity of the patho-physiological system in maintaining CNS function, circulatory function, neural-muscular function, the support that the compounds having activity in treating/prophylaxis of disorder of such diversity is lacking. Especially, per ponderous of evidence indicated that structural analogous compounds do not have 5HT2A activity, while 5HT2A active compounds do not have the instantly claimed chemical structure. Note that In re Fisher 166 USPQ 18-20 indicated that the more unpredictable the field of activity, more enablement by way of specific examples is necessary in order to establish broad claims of useful products.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang, Ph. D. whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Dec. 14, 2009

/Celia Chang/
Primary Examiner
Art Unit 1625